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1. Document ID: US 6261560 B1

L4: Entry 1 of 3 File: USPT Jul 17, 2001

US-PAT-NO: 6261560
DOCUMENT-IDENTIFIER: US 6261560 B1

TITLE: Method for inhibiting muscle protein proteolysis with an interleukin-6 receptor

DATE-ISSUED: July 17, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tsujinaka; Toshimasa	Ikoma	N/A	N/A	JPX
Ebisui; Chikara	Ikeda	N/A	N/A	JPX
Fujita; Junya	Takatsuki	N/A	N/A	JPX

US-CL-CURRENT: 424/143.1; 424/130.1, 424/139.1, 424/141.1, 424/142.1, 514/885, 514/921, 530/387.1, 530/387.9, 530/388.1, 530/388.22

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

2. Document ID: US 5639455 A

L4: Entry 2 of 3 File: USPT Jun 17, 1997

US-PAT-NO: 5639455
DOCUMENT-IDENTIFIER: US 5639455 A

TITLE: Immunosuppressant

DATE-ISSUED: June 17, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shimamura; Toshiro	Kawasaki	N/A	N/A	JPX
Nakazawa; Harumi	Kawasaki	N/A	N/A	JPX
Hamuro; Junji	Kawasaki	N/A	N/A	JPX

US-CL-CURRENT: 424/133.1; 424/130.1, 424/141.1, 424/143.1, 514/2, 530/388.23

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

3. Document ID: US 5171837 A

L4: Entry 3 of 3 File: USPT Dec 15, 1992

US-PAT-NO: 5171837
DOCUMENT-IDENTIFIER: US 5171837 A

TITLE: Peptide capable of binding interleukin 6 and an antibody against [illegible] peptide immobilized on a carrier

DATE-ISSUED: December 15, 1992

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tanihara; Masao	Kurashiki	N/A	N/A	JPX
Oka; Kiichiro	Kurashiki	N/A	N/A	JPX

US-CL-CURRENT: 530/324; 530/325, 530/326, 530/810

Full | Title | Citation | Front | Review | Classification | Date | Reference | KWIC | Draw Desc | Image

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Terms	Documents
il-6 with antibody with administration with receptor	3

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L4: Entry 2 of 3 File: USPT Jun. 17, 1

DOCUMENT-IDENTIFIER: US 5639455 A
TITLE: Immunosuppressant

BSPR:
In fact, regarding some of the above mentioned diseases, the suppression of IL-6 in mouse model experiments has led to improvement in the diseases. For example, it has been reported that, by the administration of anti-mouse IL-6 antibody or anti-mouse IL-6 receptor antibody, which have an effect of suppressing the activity of mouse IL-6, to mice inoculated with myeloma cells, it is possible to both suppress the growth of myeloma cells and raise the survival rate of the mice (Journal of Experimental Medicine, vol. 172, p. 1[illegible] (1990)); that the metastasis of tumor cells to the liver may be suppressed by the administration of anti-mouse IL-6 antibody (Japanese Journal of Cancer Research, vol. 82, p. 1294 (1991)); that even mice infected with a lethal dose of E. coli survive when they are preadministered anti-mouse IL-6 antibody which suppresses the activity of mouse IL-6 (Journal of Immunology, vol. 144, p. 4185 (1990)), that when anti-mouse IL-6 antibody which possesses mouse IL-6-suppressing activity is administered to mouse models which develop cachexia when inoculated with tumor cells, an improvement is observed not only in the weight loss, but also in the symptoms of the cachexia [illegible] (Clinical Investigation, vol. 89, p. 1681 (1992)), which thus [illegible] indicate that IL-6 is connected with the above mentioned diseases. They also indicate that if the activity of human IL-6 can be suppressed, [illegible] be provided for their treatment.

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L4: Entry 1 of 3 File: USPT Jul 17, 2001

DOCUMENT-IDENTIFIER: US 6261560 B1
TITLE: Method for inhibiting muscle protein proteolysis with antibodies to interleukin-6 receptor

DEPR:
Body weight including tumor weight, body weight excluding tumor weight (carcass weight) and gastroenemius muscle weight on day 7 after the start of the experiment are shown in FIGS. 9, 10 and 11, respectively. Increases in carcass weight and gastroenemius muscle weight were inhibited in the IL-6 receptor antibody administration group (there were no significant differences in body weight including tumor weight).

DEPR:
Cathepsin B activity and cathepsin B+L activity on day 17 of the experiment are shown in FIGS. 12 and 13, respectively. Increases in cathepsin B activity and cathepsin B+L activity observed over time were inhibited by administration of IL-6 receptor antibody (there were no significant differences observed regarding cathepsin B activity).

1: Immunol Lett 1991 Sep;30(1):17-21 Related Articles, Books

Anti-murine IL-6 receptor antibody inhibits IL-6 effects in vivo.

Suzuki H, Yasukawa K, Saito T, Anzai M, Goitsuka R, Hasegawa A, Ohsugi Y, Taga T, Kishimoto T.

Biotechnology Research Laboratory, Tosoh Corporation, Kanagawa, Japan.

Thrombopoiesis, as well as antibody production, is one of the major events in which interleukin-6 (IL-6) has been reported to be involved. Polyclonal anti-murine IL-6 receptor antibody was prepared to examine the effect of the antibody on these events in IL-6-treated mice. Administration of the anti-mIL-6R antibody inhibited the IL-6-induced increase in the number of platelets. Enhancement of the serum level of DNP-specific antibody by intraperitoneal injection of IL-6 was inhibited completely with simultaneous administration of the anti-mIL-6R antibody. The level of DNP-specific antibody was decreased, even below the basal value, by the higher dose of anti-mIL-6R antibody, indicating its effect also on endogenous IL-6. This work provides evidence that anti-IL-6R antibody inhibits IL-6 function in vivo, and provides an animal model of the therapeutic use of anti-IL-6R antibody for IL-6-related disease.

PMID: 1959939 [PubMed - indexed for MEDLINE]

1: Eur J Immunol 1992 Aug;22(8):1989-93 Related Articles, Books, LinkOut

Anti-human interleukin-6 receptor antibody inhibits human myeloma growth in vivo.

Suzuki H, Yasukawa K, Saito T, Goitsuka R, Hasegawa A, Ohsugi Y, Taga T, Kishimoto T.

Biotechnology Research Laboratory, Tosoh Corporation, Kanagawa, Japan.

Myeloma is one of the interleukin (IL)-6-related diseases to which abnormal expression of IL-6 has been reported to be linked. We examined the in vivo inhibitory effect of anti-human IL-6 receptor (IL-6R) antibody on human myeloma cell growth in mice. SCID mice were subcutaneously inoculated with solid tumor of the myeloma cell line S6B45 in which human IL-6 was acting as an autocrine growth factor. Ten intraperitoneal administrations of 100 micrograms of the anti-human IL-6R antibody PM1 at 48-h intervals strongly inhibited the growth of S6B45 cells when the administration started 24 h after tumor inoculation. The tumor growth inhibition in vivo was also observed by administration of the anti-human IL-6 antibody MH166 using the same procedure as for PM1. The inhibitory effect of PM1 was not significant when the administration started 5 or more days after tumor inoculation. This work indicates that anti-human IL-6R antibody, as well as anti-human IL-6 antibody inhibits human myeloma growth in vivo, and provides an animal model for testing the therapeutic value of agents such as antibodies to human IL-6, IL-6R and gp130, an IL-6R-associated signal transducer, in the treatment of human myelomas.

PMID: 1639101 [PubMed - indexed for MEDLINE]

1: Hybridoma 1993 Oct;12(5) 621-30

A monoclonal anti-human IL-6 receptor antibody inhibits the proliferation of human myeloma cells.

Huang YW, Vitetta ES.

Department of Microbiology, University of Texas Southwestern Medical Center at Dallas 75235.

A monoclonal antibody (UV4) against the human IL-6 receptor (hIL-6R) was generated by immunizing BALB/c mice with both a human myeloma cell line (U266) and a murine cell line (M12.4/R) transfected with the hIL-6R cDNA. Flow cytometric analysis demonstrated that UV 4 stains the hIL-6R+ cell lines U266 and U937, but not the hIL-6R- cell lines Daudi and K562. Competitive inhibition assays demonstrated that preincubation of U266 cells with UV4 inhibited the binding of a phycoerythrin (PE)-IL-6 conjugate to the hIL-6R and also inhibited the proliferative activity of IL-6 on the IL-6-dependent human myeloma cell lines ILKM2 and ILKM3. In contrast, UV4 did not interfere with the proliferation of the hIL-6R- Burkitt's lymphoma cell line, Daudi. Direct sandwich radioimmunoassays further confirmed that the UV4 bound to the same molecule as the goat anti-hIL-6R antibody. These results suggest that both UV4 and human IL-6 bind to the same or adjacent epitopes on the hIL-6R. This monoclonal antibody should facilitate studies of the structure-function relationship of IL-6R and may be useful for the treatment of IL-6-dependent diseases such as multiple myeloma.

PMID: 8300137 [PubMed - indexed for MEDLINE]

1: J Exp Med 1990 Sep 1;172(3):997-1000 Related Articles, Books

Mouse plasmacytoma growth in vivo: enhancement by interleukin 6 (IL-6) and inhibition by antibodies directed against IL-6 or its receptor.

Vink A, Coulie P, Warnier G, Renauld JC, Stevens M, Donckers D, Van Snick J.

Ludwig Institute for Cancer Research, Brussels, Belgium.

Murine plasmacytomas show a striking dependence on interleukin 6 (IL-6) for their growth in vitro. Here, we present evidence suggesting that IL-6 also plays an essential role in the in vivo development of these tumors. This conclusion is based on the finding that the tumorigenicity of an IL-6-dependent plasmacytoma cell line was increased approximately 100-fold on transfection with an IL-6 expression vector, whereas it was inhibited in animals treated with monoclonal antibodies capable of blocking the binding of IL-6 to its receptor. Injection of these antibodies 1 d before tumor challenge protected greater than 50% of the mice and retarded tumor growth in all animals. Tumors arising in antibody-treated mice retained their IL-6 dependence in vitro, suggesting that the level of protection could be improved if stronger IL-6 antagonists were available.

PMID: 2388041 [PubMed - indexed for MEDLINE]

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Mouse plasmacytoma growth in vivo: enhancement by interleukin 6 (IL-6) and inhibition by antibodies directed against IL-6 or its receptor.
J Exp Med. 1990 Sep 1;172(3):997-1000.
PMID: 2388041 [PubMed - indexed for MEDLINE]

2: Coulie PG, Vink A, Van Snick J. Related Articles

A monoclonal antibody specific for the murine IL-6-receptor inhibits the growth of a mouse plasmacytoma in vivo.
Curr Top Microbiol Immunol. 1990;166:43-6. No abstract available.
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3: Suematsu S, Hibi M, Sugita T, Saito M, Murakami M, Matsusaka T, Matsuda T, Hirano T, Taga T, Kishimoto T. Related Articles

Interleukin 6 (IL-6) and its receptor (IL-6R) in myeloma/plasmacytoma.
Curr Top Microbiol Immunol. 1990;166:13-22. Review. No abstract available.
PMID: 2073791 [PubMed - indexed for MEDLINE]

4: Matsuda T, Hirano T. Related Articles

Interleukin 6 (IL-6).
Biotherapy. 1990;2(4):363-73. Review. No abstract available.
PMID: 2268501 [PubMed - indexed for MEDLINE]

5: Hirano T. Related Articles

Interleukin 6 (IL-6) and its receptor: their role in plasma cell neoplasias.
Int J Cell Cloning. 1991 May;9(3):166-84. Review.
PMID: 2061619 [PubMed - indexed for MEDLINE]

6: Shacter E, Arzadon G. Related Articles

Elevation of IL-6 in plasma cell tumorigenesis.
AIDS Res Hum Retroviruses. 1992 May;8(5):754-6. Review. No abstract available.
PMID: 1515225 [PubMed - indexed for MEDLINE]

7: Hopkins SJ, Rothwell NJ Related Articles

Further functions of IL-6.
Immunol Today. 1991 May;12(5):170. No abstract available.
PMID: 1750926 [PubMed - indexed for MEDLINE]

8: Shimamura T, Taki S, Honda H, Yokota M, Ito S, Takahara Y. Related Articles

Analysis of interleukin 6 (IL-6)/IL-6 receptor system using monoclonal anti-IL-6 antibodies.
Mol Immunol. 1991 Nov;28(11):1155-61.
PMID: 1720500 [PubMed - indexed for MEDLINE]

9: Novick D, Shulman LM, Chen L, Revel M. Related Articles

Enhancement of interleukin 6 cytostatic effect on human breast carcinoma cells by soluble IL-6 receptor from urine and reversion by monoclonal antibody.
Cytokine. 1992 Jan;4(1):6-11.
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Exp Hematol. 1992 May;20(4):395-400.
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Development of a human interleukin-6 receptor antagonist.
J Biol Chem. 1994 Jan 7;269(1):86-93.
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13: Suzuki H, Yasukawa K, Saito T, Anzai M, Goitsuka R, Hasegawa A, Ohsugi Y, Taga T, Kishimoto T. Related Articles

Anti-murine IL-6 receptor antibody inhibits IL-6 effects in vivo.
Immunol Lett. 1991 Sep;30(1):17-21.
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Antitumor effects of IL-6 on murine liver tumor cells in vivo.
J Biomed Sci. 1999 Mar-Apr;6(2):142-4.
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17: Suzuki H, Yasukawa K, Saito T, Goitsuka R, Hasegawa A, Ohsugi Y, Taga T, Kishimoto T. Related Articles

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Eur J Immunol. 1992 Aug;22(8):1989-93.
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18: Hirano T, Akira S, Taga T, Kishimoto T. Related Articles

Biological and clinical aspects of interleukin 6.
Immunol Today. 1990 Dec;11(12):443-9. Review.
PMID: 2127356 [PubMed - indexed for MEDLINE]

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Growth autonomy and tumorigenicity of interleukin 6-dependent B cells transfected with interleukin 6 cDNA.
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A multifunctional cytokine (IL-6/BSF-2) and its receptor.
Int Arch Allergy Appl Immunol. 1989;88(1-2):29-33. Review.
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3: Suzuki H, Yasukawa K, Saito T, Goitsuka R, Hasegawa A, Ohsugi Y, Taga T, Kishimoto T. Related Articles

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J Exp Med. 1990 Sep 1;172(3):997-1000.
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Immunoassay for functional human soluble interleukin-6 receptor in plasma based on ligand/receptor interactions.
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In vivo blocking effects of a humanized antibody to human interleukin-6 receptor on interleukin-6 function in primates.
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